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Transverse flow measurement using photoacoustic Doppler bandwidth broadening: phantom and *in vivo* studies

Junjie Yao, Konstantin I. Maslov, Lihong V. Wang*
Optical Imaging Laboratory, Department of Biomedical Engineering,
Washington University in St. Louis, One Brookings Dr., St. Louis, Missouri 63130, USA

Abstract

In photoacoustic (PA) imaging of microvascular networks, the transverse component of the blood flow that is perpendicular to the acoustic probing beam is usually dominant. We propose a new method to measure the transverse flow, based on the Doppler bandwidth broadening. The bandwidth broadening is inversely proportional to the transit time spent by the absorbers passing through the focus. Because the photoacoustic signal in one A-scan has a wide band, multiple successive A-scans are used to estimate the relatively small signal variance. Then the bandwidth broadening can be calculated from the standard derivation of the Doppler spectrum. By exploiting the pulse excitation and bidirectional raster motor scanning, three-dimensional structural and flow information can be obtained simultaneously. From a flow of a suspension of carbon particles (diameter: 6 μm), transverse flow speeds from 0 to 2.5 mm/s were measured using optical-resolution photoacoustic microscopy. The bandwidth broadening at each speed was in good agreement with the theoretical prediction. The blood flow in a mouse brain was also imaged.

Keywords: Transverse flow, Doppler bandwidth broadening, Optical-resolution photoacoustic microscopy

1. INTRODUCTION

Previously, photoacoustic Doppler (PAD) shift was observed from flowing particles illuminated by an intensity-modulated continuous-wave (CW) laser beam.[1, 2] The PAD frequency shift is composed of two parts. The first part is the frequency shift of the photon density wave 'seen' by the particle as a moving receiver; the second part is the frequency shift of the resultant photoacoustic wave 'seen' by the ultrasonic transducer, where the particle works as a moving source. Usually only the second part is detectable because the wavelength of the photon density wave is much longer than that of the photoacoustic wave. Compared with other scattering-based Doppler flowmetries, such as optical Doppler tomography (ODT) and ultrasonic Doppler, PAD-based flowmetry benefits from less background noise. Moreover, PAD is independent of the illumination angle[1]. However, because a CW excitation source was used without frequency chirping, depth could not be resolved. Like the other flowmetries based on the Doppler frequency shift, PAD flowmetry was sensitive to the Doppler angle. In PA imaging of microvascular networks, the transverse component of the flow is usually dominant [Fig. 1(a)]. When the Doppler angle approaches 90º, the PAD frequency shift almost vanishes. In the current work, we propose a method to measure both the transverse flow speed based on PA Doppler bandwidth broadening and the flow direction based on bidirectional scanning.

2. METHODS

Previous works in the fields of optical coherence tomography and ultrasound imaging have demonstrated the feasibility of using the Doppler bandwidth broadening to provide quantitative information on transverse flow.[3-5] Sources of broadening include geometry, transit time, Brownian motion, velocity gradient and turbulence.[1, 3] The contributions of transit time and geometry are dominant and proved to be equivalent within the focal region.[6, 7] Because the bandwidth broadening caused by illumination is negligible, the

* Corresponding author: Lihong V. Wang, lhwang@biomed.wustl.edu

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Doppler bandwidth is determined by the two extreme photoacoustic rays emanating from a particle moving through the focal point and received by the edges of the transducer, as shown in Fig. 1(b).

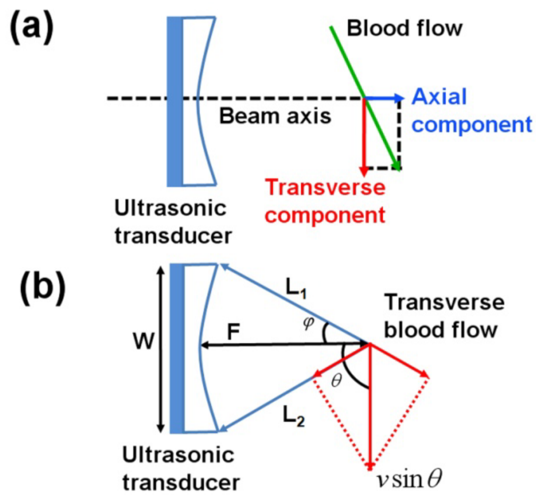

Figure 1. (a) Transverse flow is defined as the flow component perpendicular to the transducer beam axis. (b) Schematic of probe-beam geometry for the transverse flow measurement.

The Doppler bandwidth, B_d, is given by

$$B_d = f_{L_2} - f_{L_1} = 2 f_0 \frac{v}{c} \sin\theta \sin\varphi \approx f_0 \frac{v}{c} \frac{W}{F} \sin\theta \quad , \tag{1}$$

where v is the flow velocity; c is the speed of sound; θ is the Doppler angle; φ is the aperture angle of the acoustic lens; and f_0, W and F are the center frequency, the diameter, and the focus length of the ultrasonic transducer, respectively. The Doppler bandwidth is proportional to the transverse flow and is maximized when the Doppler angle is 90º. The derivation of Eq. (1) is illustrated in Fig. 1(b). The projections of the transverse flow velocity on lines L_1 and L_2 contribute to the Doppler shift in opposite signs, which results in bandwidth broadening. [8]

In the current imaging system, the sample is translated by the scanning motor. Hence, the Doppler bandwidth broadening is actually determined by the combination of the flow velocity and the motor scanning velocity. Therefore, a bidirectional scanning is used to measure the flow direction. The motor first scans with velocity $\vec{v}_{m+}$, and then switches to velocity $\vec{v}_{m-}$. $\vec{v}_{m-}$ has the same value as $\vec{v}_{m+}$ but in the opposite direction. The measured flow speeds under the two scanning directions are given by the combination speeds of the flow and the motor, and the true flow speed can be solved as follows:

$$v_f = \left[\frac{1}{2} \left(v_{f\_m+}^2 + v_{f\_m-}^2 - 2{v^2}_m \right) \right]^{1/2} \quad , \tag{2}$$

where v_{f_m+} and v_{f_m-} are the measured speeds with motor-scanning velocities $\vec{v}_{m+}$ and $\vec{v}_{m-}$, respectively; v_m is the motor scanning speed. If $v_{f\_m+} > v_{f\_m-}$, $\vec{v}_f$ must have a positive projection on

$\vec{v}_{m+}$ (i.e., $\vec{v}_f \cdot \vec{v}_{m+} > 0$) and the flow is called positive, and vice versa. Combined with the structure information, the flow direction can be measured.

3. PHANTOM STUDY

The optical-resolution photoacoustic microscopy (OR-PAM) system used in this work has been described in detail previously.[9] A straight capillary tube (inner diameter: 260 μm) and a 0.1% solution of red-dyed particles (diameter: 6 μm) were used to study the dependence of the Doppler bandwidth on the flow velocity [Fig. 2(a)]. The flow with speeds for 0 to 2.5 mm/s was controlled by a 1 mL syringe driven by a syringe pump and illuminated at 570 nm. In this instance, the bidirectional scanning was along the tube. The flow direction was the same as $\vec{v}_{m+}$.

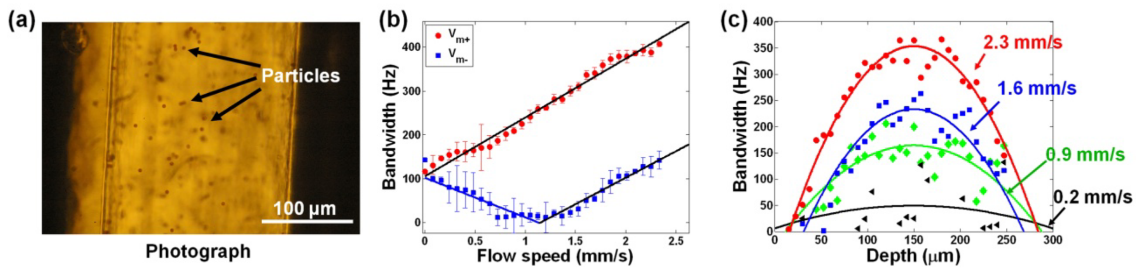

Figure 2. (a) Photograph of a straight capillary tube (inner diameter: 260 μm) filled with a 0.1% solution of red-dyed particles (diameter: 6 μm). (b) Doppler bandwidth as a function of flow velocity with a bidirectional motor scanning speed of 1.1 mm/s and Doppler angle of 90°. (c) Doppler bandwidth flow profiles along the depth direction of the tube at different flow velocities, after subtraction of the contribution of the motor scanning. Solid curves, fitted parabolic flow profiles.

We extracted the data from the center of the capillary [Fig. 2(b), $\theta = 90^\circ$]. When the flow velocity was zero, the bandwidth broadening was caused only by the motor scanning. When the scanning was in the same direction as the flow ($\vec{v}_{m+}$), the bandwidth increased as the flow speed increased. When the scanning was opposite to the flow ($\vec{v}_{m-}$), the bandwidth first decreased as the flow speed increased. However, when the flow speed exceeded the scanning speed, the bandwidth began to increase. The turning point indicated the motor-scanning speed v_m. After subtraction of the contribution of the motor scanning, the bandwidth profiles at the different speeds are shown in Fig. 2(c). A parabolic flow model was used to fit the experimental results (solid curves).

4. *IN VIVO* STUDY

Blood flow in a mouse brain was also imaged. Before experiment, a Swiss Webster mouse (Hsd:ND4, 25–30 g; Harlan, Indianapolis, IN) was anesthetized by intraperitoneally administering a dose of 80 mg/kg ketamine and 10 mg/kg xylazine. A cranial window [~2 mm × 2 mm, Fig. 3(a)] was made using a dental drill. A volumetric dataset was acquired under bidirectional scanning at 560 nm and 570 nm on a 1 mm × 1 mm area [Fig. 3(b)]. The A-scan repetition rate was ~1.5 KHz.

Because 570 nm is an isosbestic point, the PA signal acquired at this wavelength maps the total hemoglobin concentration, which provides structural information of the vasculature. The maximum-amplitude projection (MAP) images are shown in Figs. 3(a) and (b). The dual-wavelength measurements were used to calculate oxygen saturation (SO_2) using a previously published method [10] [Fig. 3(c)]. The vessels with high SO_2 values (>90%) are believed to be arterioles (shown in red), whereas the vessels with SO_2 values as low as 60–80% are most likely to be venules (shown in green). Bidirectional measurements at 570 nm were used to calculate the Doppler broadening of bandwidth, which provided the transverse blood flow speed image [Fig. 3(d)]. Eight sequential A-scans in one B-scan were averaged to increase the detection sensitivity to velocity. The arterioles have faster flow speed than the venules, and the flow speeds decrease from parent vessels to daughter vessels.

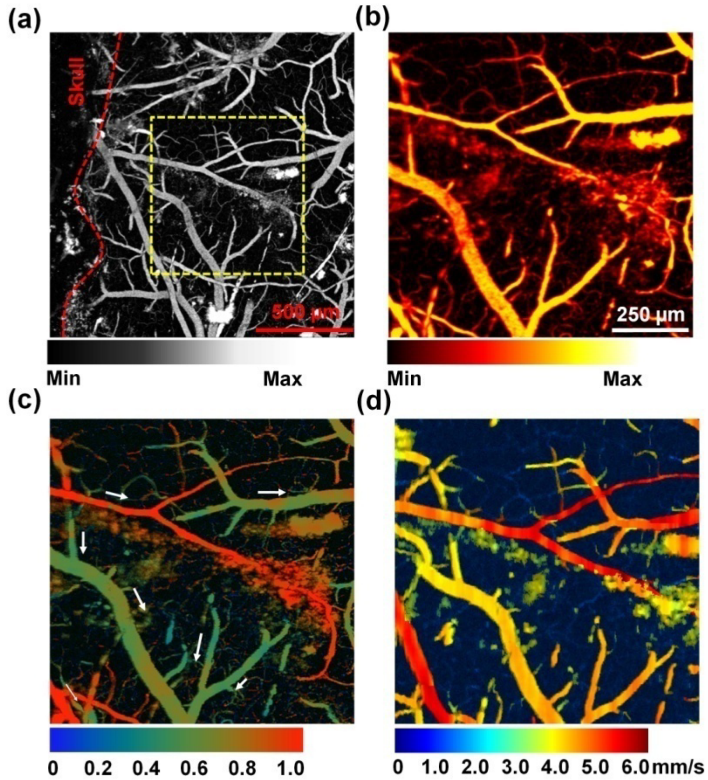

Figure 3. (a) PA image of the vascular network in a mouse brain. (b) Closeup of the area indicated by the dashed box in (a). (c) Oxygen saturation image based on a dual-wavelength measurement under 560 nm and 570 nm. The arrows indicate the blood flow directions. (d) Blood flow speed image based on Doppler bandwidth broadening measurement.

5. CONCLUSION

In summary, we have demonstrated a new method that uses PA Doppler broadening of bandwidth to measure transverse blood flow. By the use of dual-wavelength excitation and bidirectional scanning, structural, oxygenation, and flow information can be obtained simultaneously in the same system.

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